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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/596,444	06/19/2000	Wei Huang	LJL 354B	4000

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EXAMINER	
LAM, ANN Y	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 01/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/596,444	HUANG ET AL.	
	Examiner	Art Unit	
	Ann Y. Lam	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 October 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,7-10,12,17 and 47-60* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,7-10,12,17 and 47-60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7, 8, 56 and 57 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 7, lines 3-4, and 56 lines 2-4, recites the limitation "the formation of unlabelled phosphorylated protein". There is insufficient antecedent basis for this limitation in the claim.

Claims 8 and 57 are vague because it is not clear as to the function of the phosphorylated protein in the method of claim 1. Claim 1 has been amended to remove any recitation of a protein. The claim is also not clear as to how the binding partner can bind specifically to the protein without regard to the amino acid sequence of the protein. Any binding partner will work?

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-3, 8, 9, 12, 17 and 60 are rejected under 35 U.S.C. 102(e) as being anticipated by Nikiforov, 6,287,774.

As to claim 1, Nikiforov discloses a method of detecting addition or removal of a phosphate group to or from a substrate (col. 13, lines 40-42, and lines 47-50), comprising contacting a luminescent peptide (i.e., fluorescently labeled phosphorylatable substrate 302, col. 13, line 20) with a binding partner (i.e., polycation, col. 13, line 26) that binds specifically to the peptide only if the peptide is phosphorylated (col. 13, lines 29-30), wherein the binding partner includes an entrapped metal (col. 13, line 35) that selectively binds to phosphorylated peptides, and wherein the peptide is a substrate (302, col. 13, line 20) for an enzyme (i.e., kinase enzyme 306, col. 13, line 20) that catalyzes addition or cleavage of a phosphate group to or from a protein (col. 13, lines 19-21), and measuring luminescence polarization from the luminescent peptide (col. 6, lines 1-5), wherein the amount of measured luminescence polarization can be related to the extent of binding between the luminescent peptide and the binding partner (col. 6, lines 1-12.)

As to claim 2, the step of correlating the measured luminescence polarization with kinase activity is disclosed (col. 6, lines 1-12, and col. 7, lines 27-31, and col. 13, lines 19-26.)

As to claim 3, phosphatase activity is determined (col. 13, lines 59-66).)

As to claims 8, the binding partner binds specifically to a phosphorylated protein substantially without regard to the particular amino acid sequence of the protein (col. 13, lines 29-21.)

As to claim 9, the binding partner (i.e., polycation, col. 13, line 26)) comprises a macromolecule that includes entrapped metal ions.

As to claim 12, the peptide is amidated on one end (col. 7, lines 29-32.)

As to claim 17, the step of measuring luminescence polarization includes illuminating the sample with polarized light (col. 5, line 13.)

As to claim 60, the method further comprises contacting at least one of the luminescent peptide and the enzyme with a candidate modulator phosphate 304, col. 13, line 21), prior to the step of measuring luminescence polarization.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1. Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nikiforov, 6,287,774.

Nikiforov discloses the invention substantially as claimed (see above), except for the peptide being no more than about 15 amino acids.

However, it would have been obvious to one of ordinary skill in the art at the time the invention was made to perform the Nikiforov assay using a peptide that is no more than about 15 amino acids since this is an optimum or workable range and it has been held that where the general conditions of a claim are disclosed in the prior art, as it is in the case at hand, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 1-5 USPQ 233.

2. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nikiforov, 6,287,774, in view of de Sauvage et al., 6,022,708.

De Sauvage discloses a method of detecting addition or removal of a phosphate group to or from a substrate (column 32, lines 56-58), comprising contacting a luminescent peptide (i.e., the "substrate", column 32, line 58) with a binding partner (i.e., "antibody", column 33, line 11) that binds specifically to the peptide only if the peptide is phosphorylated (column 33, lines 11-12), or only if the peptide is not phosphorylated, wherein the peptide is a substrate (i.e., "kinase substrate", column 32, line 53) for an enzyme that catalyzes addition or cleavage of a phosphate group to or from a protein (column 32, lines 53-55.)

However, de Sauvage does not disclose that the assay is a competitive assay comprising catalyzing the formation of unlabelled phosphorylated protein to competitively bind to the binding partner.

De Sauvage discloses that various diagnostic assay techniques known in the art may be used, such as competitive binding assay, direct and indirect sandwich assays (column 28, lines 63-64.)

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize competitive binding assay as taught by de Sauvage in the Nikiforov assay method because de Sauvage teaches that competitive assays are an obvious alternative to the direct assay of Nikiforov to detect addition or removal of phosphate groups from a substrate.

3. Claims 47-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nikiforov, 6,287,774, in view of Fuller, 5,424,190.

Nikiforov discloses the invention substantially as claimed (see above). More specifically, Nikiforov discloses examples of binding pairs substrates and enzymes (col. 7, lines 19-31.) However, Nikiforov does not disclose a stop solution including a chelator, and except for the steps of contacting and measuring being performed in a microplate well.

Fuller teaches a stop solution such as EDTA which comprises a chelator useful to inactivate enzymes prior to analysis of the product of the enzymatic reagents (col. 1, lines 13-15 and 24-40, and col. 2, line 18, and lines 30-34.)

It would have been obvious to one of ordinary skill in the art at the time the invention was made to provide EDTA as a stop solution as taught by Fuller in the

Nikiforov enzymatic assay method because Fuller teaches that such solution is conventionally used to inactive enzymes desirable for stopping a reaction in an enzymatic assay providing the advantage of facilitating subsequent analysis of the product of the enzymatic reagents in the Nikiforov assay.

Fuller also teaches use of a microtiter plate (which are known to have wells) for performing the assay reactions (col. 2, lines 36-38.)

It would have been obvious to utilize a microplate well as taught by Fuller in the Nikiforov assay method as a well known and conventional means to hold reagent and stop solutions as would be desirable for performing an assay.

4. Claims 10, 50-52, 54, 55, 57 and 59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nikiforov, 6,287,774, in view of Haber et al., 4,421,435.

Nikiforov discloses the invention substantially as claimed (see above). More specifically, Nikiforov teaches that the assay method comprises contacting a kinase enzyme and phosphorylatable substrate in the presence of phosphate. The reaction yields the phosphorylated product, which is then contacted with a polycation which associates with the negatively charged phosphorylated product, which drastically affects the rotational diffusion rate. The polyionic component may be a large molecule that has associated therewith multivalent metal cations. Nikiforov discloses some examples of multivalent metal cations for binding with a phosphorylated substrate or other groups bearing oxygen, nitrogen or sulfur groups which imparts a significant binding affinity towards phosphorlyated substrates, slowing rotation diffusion rate of the product, which

can be detected (col. 13, lines 19-46.) However, Nikiforov does not list gallium as one of the examples of such multivalent metal cation.

Haber et al. teaches that gallium is a multivalent cation which be coupled to a protein molecule for diagnostic purposes (col. 2, lines 21-24.) It would have been obvious to one of ordinary skill in the art at the time the invention was made to specifically utilize gallium cation as taught by Haber et al. because such a multivalent metal cation, which is generally taught by Nikiforov, provides the advantage of binding to a phosphorylated substrate, which slows the rotation diffusion rate of the phosphorylated substrate, allowing for verification of phosphorylation of the substrate, as taught by Nikiforov.

5. Claim 56 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nikiforov, 6,287,774, in view of Haber et al., 4,421,435, and further in view of de Sauvage et al., 6,022,708.

Nikiforov in view of Haber et al. discloses the invention substantially as claimed except for the assay format being competitive binding format.

De Sauvage discloses a method of detecting addition or removal of a phosphate group to or from a substrate (column 32, lines 56-58), comprising contacting a luminescent peptide (i.e., the "substrate", column 32, line 58) with a binding partner (i.e., "antibody", column 33, line 11) that binds specifically to the peptide only if the peptide is phosphorylated (column 33, lines 11-12), or only if the peptide is not phosphorylated,

wherein the peptide is a substrate (i.e., "kinase substrate", column 32, line 53) for an enzyme that catalyzes addition or cleavage of a phosphate group to or from a protein (column 32, lines 53-55.)

De Sauvage discloses that various diagnostic assay techniques known in the art may be used, such as competitive binding assay, direct and indirect sandwich assays (column 28, lines 63-64.)

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize competitive binding assay as taught by de Sauvage in the Nikiforov/Haber et al. assay method because de Sauvage teaches that competitive assays are an obvious alternative to the direct assay of Nikiforov to detect addition or removal of phosphate groups from a substrate.

6. Claims 53 and 58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nikiforov, 6,287,774, in view of Haber et al., 4,421,435, and further in view of Fuller, 5,424,190.

Nikiforov in view of Haber et al. discloses the invention substantially as claimed (see above). More specifically, Nikiforov discloses examples of binding pairs substrates and enzymes (col. 7, lines 19-31.) However, Nikiforov does not disclose a stop solution including a chelator, and except for the steps of contacting and measuring being performed in a microplate well.

Fuller teaches a stop solution such as EDTA which comprises a chelator useful to inactivate enzymes prior to analysis of the product of the enzymatic reagents (col. 1, lines 13-15 and 24-40, and col. 2, line 18, and lines 30-34.)

It would have been obvious to one of ordinary skill in the art at the time the invention was made to provide EDTA as a stop solution as taught by Fuller in the Nikiforov/Haber et al. enzymatic assay method because Fuller teaches that such solution is conventionally used to inactive enzymes desirable for stopping a reaction in an enzymatic assay providing the advantage of facilitating subsequent analysis of the product of the enzymatic reagents in the Nikiforov/Haber assay.

Fuller also teaches use of a microtiter plate (which are known to have wells) for performing the assay reactions (col. 2, lines 36-38.)

It would have been obvious to utilize a microplate well as taught by Fuller in the Nikiforov/Haber et al. assay method as a well known and conventional means to hold reagent and stop solutions as would be desirable for performing an assay.

Response to Arguments

Applicant's arguments with respect to the above rejected claims have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ann Y. Lam whose telephone number is 571-272-0822. The examiner can normally be reached on M-Sat 11-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

A.L.

Christopher L. Chin

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1/21/05